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Original Article

Evaluation of Haematological Variables in Patients with Typhoid in Pakistan

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ABSTRACT

Typhoid fever results in significant hepatic problems and biochemical abnormalities. The most effective diagnostic procedure now is the bacterial culture, but serologic tests are still often used, and a speedy and accurate diagnostic test for typhoid fever is still required. **Objectives:** To examine the haematological parameters between typhoid patients and healthy individuals to find any distinctive parameters that could be used as typhoid fever diagnostic indicators. **Methods:** This study set out to compare haematological changes in 550 patients with 550 healthy persons. **Results:** We found low hemoglobin (8.95±1.43), low hematocrit (32.62±5.38), high ESR (53.89±9.21), high platelet count (482003±86792), high WBCs count (14464±1694), high neutrophil percentage (63.60±9.26), low lymphocyte percentage (25.33±2.93), and high NLCR (2.498±0.45) against the healthy control group. **Conclusions:** This distinctive pattern can be easily obtained using a minimally invasive method and used to diagnose typhoid fever.

INTRODUCTION

A widespread bacterial infection known as typhoid fever is brought on by *Salmonella* typhi. It is a contagious illness that spreads orally and is brought on by ingesting contaminated food and drink by the faces or urine of infected persons[1]. Typhoid typically presents with fever, headache, stomach pain, relative bradycardia, and splenomegaly as its initial symptoms[2]. The first week is characterized by toxicity, high fever, and constipation; the second week is characterized by diarrhea; the third week is characterized by splenomegaly, bone marrow findings, and other complications such intestinal bleeding and perforation[3]. Typhoid annually results in 16.6 million new infections and 600,000 fatalities, making it a major cause of illness and mortality globally. Nearly 80% of cases and fatalities take place in Asia. Although the prevalence has been declining, rare outbreaks sometimes happen, especially during the hot months[4-6]. Only human being can transmit typhoid disease, and low- and middle-income nations have the highest risk of infection with endemic typhoidal *Salmonella*, inadequate sanitation, and limited access to safe food and water[7]. The majority of Typhi infection serotypes are identified solely based on clinical criteria and are presumed to be treatable. Typhoid fever presents with a variety of symptoms that are similar to those seen with other febrile illnesses in many places where this disease is common, making a clinical diagnosis challenging[8]. *Salmonella enterica* serotype Typhi must be isolated and identified in a lab to treat typhoid disease. The most reliable way to determine whether you have an infection is to isolate *Salmonella* from your blood, urine, or

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stool[9]. The typical diagnostic procedure is blood culture, which is successful in 60 to 80% of cases [10]. However, patients frequently use antibiotics in our nation before receiving a medical diagnosis, therefore only 40% to 60% of the time bacteria can be isolated from blood cultures. After the first week, the likelihood of a positive blood culture declines, and the fourth week is when it turns negative [11]. Stool culture is also a crucial technique for locating; whenever a blood culture is negative, it might be certain. Although using a duodenal string to culture the upper GI tract can be helpful, people do not respond well to the operation [10,12]. Typhoid fever can be diagnosed and its prognosis evaluated using haematological abnormalities[13,14]. The goal of this study was to examine the haematological parameters between typhoid patients and healthy individuals to find any distinctive parameters that could be used as typhoid fever diagnostic indicators.

METHODS

A cross-sectional study was conducted on a total of 1100 people, 550 with typhoid fever and 550 healthy controls. Only individuals whose diagnosis of typhoid fever was confirmed based on the typhidot test were included in the study. Their venous blood was drawn into plain vacutainers for the serum and vacutainers containing EDTA for whole blood. Since this is a retrospective, patient consent was not requested. Typhidot tests were performed on serum samples after centrifuging for 10 minutes at 6000 rpm at 4°C[15,16]. Blood culture media was mixed with 5 ml of the patient's blood, and the blood culture bottles were incubated for 7 days at 37 °C. The subculturing of broth was performed on blood agar and MacConkey agar after 48 and 72 hours. The following day, by employing gram staining and traditional biochemical methods, isolates were identified. The modified Kirby-Bauer disc diffusion method was used for assessing the susceptibility to ampicillin (17 mm), chloramphenicol (18 mm), ceftriaxone (21 mm), tetracycline (19 mm), ofloxacin (16 mm), norfloxacin (17 mm), ciprofloxacin (21 mm), and nalidixic acid (19 mm). Gentamicin were used to treat the strains that are resistant to ampicillin and trimethoprim (15 mm)[17,18]. Utilizing the TyphiDot (CTK) quick diagnostic kit finds IgM or IgG antibodies in patient's samples. CRP levels were determined utilizing an Aeroset 2.0 analyzer and an automated enzyme-linked immunoassay (ELISA) (Abbott Diagnostics, USA). A Sysmex XE-2100 hematology analyzer was used to perform CBC (Sysmex Corporation, Kobe, Japan). By division of the neutrophil percentage by the lymphocyte percentage, the neutrophil to lymphocyte cell ratio (NLCR) was determined [7]. Hematocrit, platelet, hemoglobin, erythrocyte sedimentation rate (ESR), lymphocyte, WBCs, and neutrophil percentage, and NLCR are among the hematological markers included. Data visualization and statistical analysis were carried out using GraphPad Prism 9, and t test was performed to see if there was a significant statistical difference between patient and control group.

RESULTS

This study enrolled 550 patients and 550 healthy adults at District Headquarters Hospital and Allied Hospital, Faisalabad. The predominant clinical symptoms in typhoid patients at the time of sample collection were fever, toxic and sick appearance, relative bradycardia, anemia, abdominal tenderness, hepatomegaly, splenomegaly, and jaundice. Graphical presentation of all parameters is provided in the form of box plot graph (Figure 1). In typhoid patients, hemoglobin levels were found to be low (mean ± SD, 8.95±1.43) against the healthy control group (12.48±1.82), The hematocrit level was found to be low (32.67±5.38) versus a healthy control group (39.21±3.61). The ESR readings of those suffering from typhoid fever differed significantly from those of the control group. The mean ESR value in typhoid patients was high (53.89±9.21) in comparison to healthy control group (13.99±6.13).

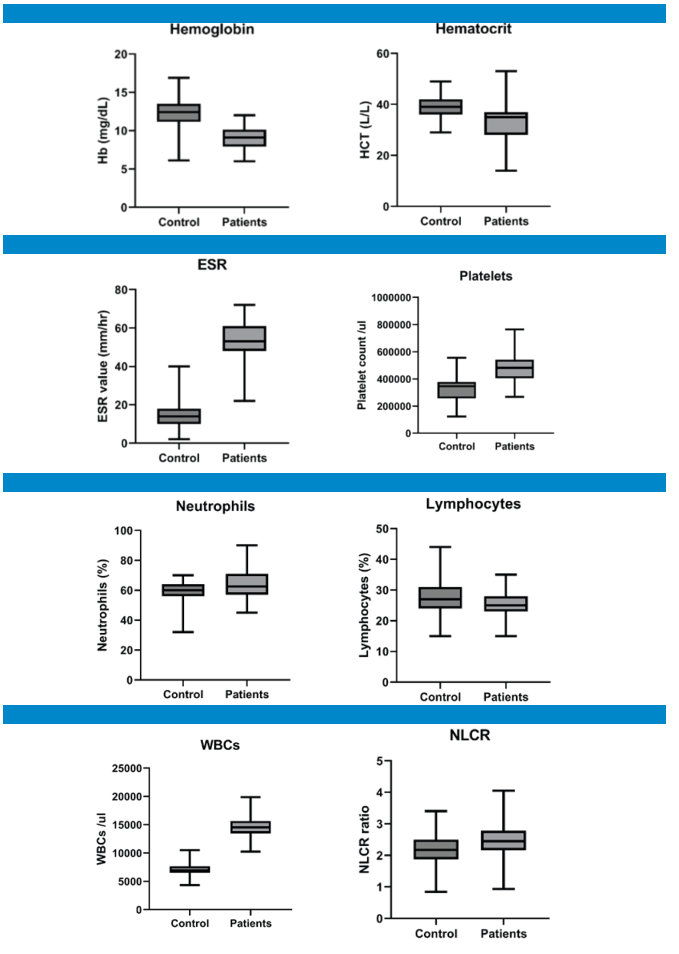

Figure 1: Graphical presentation of hematological parameters.

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Typhoid patients have a high platelet count (482003±86792) when compared to the healthy group (310502±80433). Similarly, the WBC count was considerably higher in the research (14464±1694) in contrast to a healthy control group (1721±1245). In typhoid patients, the neutrophil percentage was high (63.60±9.26) against the healthy group (59.76±6.29), and the percentage of lymphocytes in the study was lower; (25.33±2.93) and (28.01±4.81) in typhoid patients versus a healthy comparison group. NLCR ratio in typhoid fever was high (2.5±0.45) against the healthy group (2.2±0.44). With a p-value of 0.05, the results of all haematological parameters were statistically significant.

DISCUSSION

Typhoid fever is a multi-stage, complex condition that has several stages . Bacteria invade macrophages and spread throughout the reticuloendothelial system during the asymptomatic incubation phase. Hematological problems, such as anemia, thrombocytopenia, eosinophilia, and disseminated intravascular coagulation (DIC), are usually brought on by typhoid fever. Hemophagocytosis and bone marrow suppression are just two of the mechanisms involved in the creation of these haematological changes. In normal practice, older markers including C-reactive protein (CRP), neutrophil differential count, and WBCs are still the most often used markers of infection to identify typhoid fever . Numerous haematological parameter abnormalities were discovered in comparison to the healthy control. According to a paper by Eissa et al. among typhoid patients, platelets count was considerably higher in patients with typhoid fever than in the control group . Like that, these typhoid patients had high ESR values. In 2015, 100% of cases with Salmonella myocarditis were reported with the same high ESR levels . According to the earlier report, also patients' hemoglobin levels were lower than normal in this current study . We discovered that typhoid patients had higher leucocyte counts. Additionally, in the differential leucocyte count, patients had high neutrophil percentages and low lymphocyte percentages. Previous studies have found that under a variety of stressful circumstances, neutrophil levels rise while lymphocyte counts fall. Increased neutrophil numbers are caused by demargination, delayed neutrophil apoptosis, and growth factors' activation of stem cells, whereas lymphocytopenia is caused by lymphocyte redistribution, margination within the lymphatic system, and is distinguished by an increase in apoptosis . Following their discovery of the clinical utility of lymphocytopenia as a marker to diagnosis bacteremia in emergency rooms, Wyllie et al. concluded that lymphocytopenia is a predictor of bacteremia in typhoid fever patients as well . In many clinical circumstances, the NLCR parameter has been discovered to be a rather straightforward marker . Additionally, when compared to the neutrophil, WBC, and CRP levels, this measurement has been used to predict bacteremia in infectious emergency admissions as a simple infection marker . In addition, individuals admitted with Salmonella Typhi infection had higher NLCR levels. By demonstrating that typhoid fever patients have a significant level of this marker, and that it may help with typhoid diagnosis as well as later evaluation of the prognosis and severity of typhoid fever, our work contributes to previous findings. The NLCR can be calculated easily and doesn't need any additional testing. Applying the NLCR can be done with the help of metrics that are already available, such as the WBC count, neutrophil, and lymphocyte percentages from the CBC count. With the NLCR, typhoid diagnosis is substantially more beneficial. This research has several restrictions. Firstly, since this study was conducted only in Faisalabad, the results need also be confirmed in other cities. Secondly, more research on typhoid fever needs to be done in a different prospective validation study with more patients. Thirdly, malnutrition, factors that trigger apoptosis or can influence cell maturation due to bone marrow hypoplasia are only a few of the numerous factors other than infection that can cause lymphocytopenia –. Future research should take this issue into consideration since it was not perceived by study participants as a complicating factor for lymphocytopenia in our study. Fifth, the best method for identifying typhoid fever was positive blood cultures. However, getting the right volume of blood for culture and timing blood samples in relation to the start of antibiotic treatment are also error-prone aspects of blood culture . Additionally, this retrospective analysis did not assess compliance with the blood sample protocols outlined in local lab manuals; this compliance must now be assessed in a prospective validation study. These markers are inexpensive and simple to incorporate into routine practice, and aid in making the diagnosis as well as predicting morbidity and assisting with management strategy. The haematological alterations and liver involvement, despite their great incidence and seriousness, are only temporary. Typhoid infection can be identified using lymphocytopenia. Additionally, the NLCR has even greater relevance in the diagnosis of typhoid fever. This marker is straightforward, simple to calculate and obtain, simple to integrate into daily practice, and free of additional fees.

CONCLUSIONS

Significant changes in haematological parameters are caused by typhoid disease. Platelet count, ESR, and WBC

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count were all above average. Both hematocrit and hemoglobin were below the normal range, and high neutrophil percentage and low lymphocyte percentage led to elevated NLCR in typhoid fever patients. Typhoid fever can be diagnosed using this distinguishing pattern of haematological data, which is simple to get by a minimally invasive method.

Conflicts of Interest

The authors declare no conflict of interest

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